REMARKS

In view of the preceding amendments and the comments which follow, and pursuant to 37 CFR §1.111, amendment and reconsideration of the Official Action of May 24, 2004 is respectfully requested by Applicants.

Claims 2, 3, 6-10, 12, 14, 17, 19, and 21 have been canceled. Claims 1, 4, 5, 11, 13, 15, 16, 18, and 20 have been amended. New claim 22 has been added. Support for amended language is found in the originally filed specification and claims. No new matter has been added. New claim 22 is a dependent claim that parallels claim 4 except that the recitation is with regard to the β subunit rather than the α subunit.

Description of the drawings

The Examiner has remarked that the specification does not contain a brief description of the drawings as required by 37 CFR §1.74.

Applicants direct the Examiner's attention page 28, lines 1-6, of the specification which describe Figure 1. Figure 2 is described on page 31, lines 1-8, and Figure 3 is described on page 32, lines 16-21. These descriptions comply with the requirements of 37 CFR §1.74.

Rejection under 35 USC §112, second paragraph

Claims 1, 11, 13, 15, 16, 18, 20, and 21 have been rejected under 35 USC §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. The Examiner argues that:

1. Claims 1, 15, 20, and 21 are indefinite in the recitation of "AMV-RT". Applicants have overcome the rejection by amending Claim 1 to recite "avian myeloblastosis virus reverse transcriptase" prior to the first occurrence of "AMV RT".

2. Claims 1 and 16 are indefinite in the recitation of "and/or". This rejection is overcome by the present amendment which eliminates the recitation.

3. Claim 1 is confusing and apparently incorrect in the recitation of "transformed in". This rejection is overcome by the present amendment, and claim 1 now recites "transforming...into".

4. Claim 11 is indefinite in that there is no antecedent basis for "the tryptophan tRNA". The present amendment overcomes this rejection by reciting "tryptophan tRNA".

5. Claim 13 is indefinite in the recitation of "GroEL and GroES, Dnak and DnaJ, GrpE and/or ClpB". It is impossible to tell how many of the 6 genes are meant to be expressed. This rejection is overcome by the present amendment whereby Claim 13 now recites that the chaperone gene is "selected from the group consisting of GroEL, GroES, Dnak, DnaJ, GrpE, and ClpB".

6. Claim 18 is confusing and indefinite in the recitation of "expressed in a prokaryotic host cell". It is not clear whether the prokaryotic cells of claim 1 are intended or some unrelated cell. The present amendment eliminates the recitation "expressed in a prokaryotic host cell" to overcome the rejection.

7. Claim 21 is objected to as being in improper form. As Claim 21 has been canceled, this rejection is now moot.

The present amendment having now overcome the rejections under 35 USC 112, second paragraph, Applicants respectfully request the Examiner's reconsideration.

Rejection under 35 USC §112, first paragraph

Claims 1-20 have been rejected under 35 USC §112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was

not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The Examiner argues that it appears from a reading of the specification that a helper plasmid must be used in order to express the α and β genes. pAMV-αlacIq and pAMV-βdnaY are the expression plasmids used to express AMV-α and AMV-β, with the lacIq and dnaY expression cassettes coming from the helper plasmids (Examples 2 and 3). These combinations were shown to produce an active reverse transcriptase (Figure 1). This is the apparent difference in the results of Swaminathan, where they apparently obtained 90% insoluble component and the instant application (page 25, lines 19-20 of Swaminathan). Therefore the instant claims should be limited to the embodiments shown in the specification to produce active enzymes.

The Examiner remarks that E. coli LE392 pAMVαβ-4+pCHAP-5 cells described in Example 6 might be shown to produce an active reverse transcriptase but this is not fully understood. Figure 3 is purported to show this activity, but lanes 2, 4, and 5 show increasing amounts of "amplification product", yet they have decreasing amounts of product. An explanation is required.

Applicants respond first with regard to Example 6 and Figure 3. Lanes 1, 2, 4, and 5 do not show an increasing amount of amplification product but rather show successful PCR amplification of several different reaction products, i.e., different fragments of the human dystrophin gene which range from 8 kb to 13.5 kb, using the recombinant AMV RT of the invention. Thus, Example 6 demonstrates not only the production of an active reverse transcriptase, but of an active reverse transcriptase that is effective even with longer DNA fragments.

Applicants assert that the rejection has now been overcome, and the Examiner's reconsideration is respectfully requested.

Rejection under 35 USC §103 (a)

Claims 1-20 have been rejected under 35 USC §103 (a) as being unpatentable over either of Swaminathan, N., WO 00/42199, July 20, 2000 (hereinafter "Swaminathan") or Mueller, et al., J. Biol. Chem. 264:24, 13975-13978, 1989 (hereinafter "Mueller").

The Examiner argues that Swaminathan teaches the cloning of the genes for avian myeloblastosis virus reverse transcriptase into *E. coli* and the expression of an active enzyme. While it is true that page 25, lines 19-20, teach about "90% of the expressed protein was found in inclusion bodies," there was produced 10% that was soluble. It is noted that the instant claims do not require a soluble enzyme, and that there is nothing teaching that the enzyme present in the inclusion bodies did not have activity. It would have been obvious to one of ordinary skill in the art to use the methods taught by Swaminathan to clone AMV RT with at least a reasonable expectation of success. The requirements of the dependent claims would have been obvious to one of ordinary skill, absent convincing proof to the contrary.

The Examiner argues that Mueller teaches the cloning of the heterodimer of HIV reverse transcriptase into *E. coli* and the production of an active product. Since it is known that HIV reverse transcriptase is a heterodimer like AMV RT, it would have been obvious to one of ordinary skill in the art to use the methods taught by the instant reference to clone AMV RT with at least a reasonable expectation of success since both enzymes are heterodimers. The requirements of the dependent claims would have been obvious to one of ordinary skill, absent convincing proof to the contrary.

In rebuttal, Applicants argue that the case for *prima facie* obviousness has not been made. By way of the present amendment, Claim 1 and Claims 4, 5, 11, 13, 15, 16, 18, 20, and 22 depending therefrom specifically recite that the cloning step includes a lacIq gene and a dnaY gene. The use of the lacIq and dnaY genes are not taught or

suggested by by Swaminathan, nor does Swaminathan provide a motive to try these genes. Furthermore, Swaminathan actually teaches away from the use of prokaryotic cells such as E. coli, as recited in Applicants claims. On page 28, line 11, Swaminathan teaches that the Baculoviral system (eukaryotic) is preferred for expression of RT and fragments thereof. At lines 14 and 15, Swaminathan teaches that the RT polypeptides from eukaryotic cells were most active and stable while the polypeptides from prokaryotic cells were less active and stable.

Mueller teaches the expression of the heterodimer of HIV RT; however, Applicants argue that a reasonable expectation of success is missing if one were to apply Mueller's teachings to the expression of AMV RT. The differences between the two enzymes are biologically significant. As taught by Swaminathan on page 4, the HIV heterodimer comprises a 66 kDa β polypeptide and a 51 kDa α polypeptide, while the avian RT heterodimer consists of a larger 95 kDa β polypeptide and a 63 kDa α polypeptide. Furthermore, the HIV RT α polypeptide lacks RNase H activity and the HIV RT β polypeptide lacks the integrase activity of avian RT β polypeptides. Moreover, like Swaminathan, Mueller also fails to teach or suggest or provide the motivation to try including the helper genes lacIq and dnaY.

For the foregoing reasons, Applicants argue that the case for *prima facie* obviousness has not been made, and they respectfully request the Examiner's reconsideration of the rejection.

Applicants submit that their application is now in condition for allowance, and favorable reconsideration of their application in light of the above amendments and remarks is respectfully requested. Allowance of claims 1, 4, 5, 11, 13, 15, 16, 18, 20, and 22 at an early date is earnestly solicited.

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The Examiner is hereby authorized to charge any fees associated with this Amendment to Deposit Account No. 02-2958. A duplicate copy of this sheet is enclosed.

Respectfully submitted,

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